Effect of 2% Minocycline Hydrochloride Ointment in The Treatment of Periodontitis Patients: A Pilot Study

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Abstract

To evaluate the efficacy of local drug delivery of 2% Minocycline Hydrochloride (HCL) ointment as an adjunctive in non-surgical periodontal treatment. This pilot study, a clinical trial, included 9 periodontitis patients who completed the hygienic phase of periodontal treatment and enrolled in supportive periodontal therapy. All of the participants had two or more sites of remaining periodontal probing depth (PPD) $\geq$ 5 mm in bilateral quadrants. Twenty-two sites were selected and randomly allocated for 2% Minocycline HCL ointment application (test group) and non-application (control group) with a split-mouth design. 2% Minocycline HCL ointment was applied in 11 sites of PPD at days 0, 14, and 28. The clinical parameters; PPD, gingival margin (GM), and clinical attachment level (CAL) were recorded at the baseline and evaluation (4 weeks after last application) in both groups. There was no statistically significant difference in PPD and CAL at the baseline between the control and the test group. The test group showed a significantly greater reduction in PPD and CAL gain between the baseline and evaluation. The PPD reduction in the control groups between the baseline and evaluation revealed a statistically significant difference. However, no statistically significant difference in CAL gain was observed between the baseline and evaluation in the control group. The data suggested that subgingival administration of Minocycline ointment after non-surgical periodontal treatment might be helpful in PPD reduction and CAL gain within the first month after administration.

Keywords: *Local antibiotics, Adjunctive periodontal treatment, Efficacy, Pilot study, 2% Minocycline Ointment*

1. Introduction

The etiology of periodontal disease is bacterial biofilm. The ultimate key for treating periodontal disease is to eradicate pathogenic bacteria and return the periodontium to homeostasis. Periodontal instrumentation by a technique of scaling and root planing (SRP) significantly reduces the microbial load from the periodontal pocket and tissues. However, the instrument might not be able to remove the deposits in pockets deeper than 6 mm, which has led to the development of adjunctive periodontal treatment.

In adjunctive periodontal treatment, systemic antibiotics, for example; Amoxicillin, Metronidazole, and Tetracycline have been frequently used for improving the effectiveness of healing following the SRP. Systemic antibiotics are recommended when the remaining pocket depth is deeper than 6 mm. The biggest drawback of systemic antibiotics is antibiotic resistance. Because of this disadvantage, the development of local antibiotics was being introduced as an alternative treatment option to adjunctive periodontal therapy.

Currently, many locally delivered antibiotics have been being manufactured into different forms, for example, Clarithromycin, Metronidazole, Minocycline, Tetracycline, Doxycycline, Moxifloxacin. One of the most commonly used antibiotics is Minocycline, because of its specificity towards periodontal pathogens. There are two forms of Minocycline delivery; Minocycline microspheres (Arestin®) and gel (Periocline®). In this present study, 2% Minocycline Hydrochloride (HCl) ointment is addressed due to its accessibility worldwide and cost-effective approach for participants.

2. Objectives

To evaluate the efficacy of local delivery of 2% Minocycline HCL ointment in periodontal probing depth reduction and clinical attachment level gain in periodontitis participants who were enrolled in supportive periodontal treatment.

3. Materials and Methods

The ethical approval of the study was provided by the Ethical Committee Board of Rangsit University (RSUERB2020-046). Seventeen participants with chronic periodontitis who had undergone active periodontal treatment (full mouth SRP, oral hygiene instruction, full mouth reSRP, re-evaluation of periodontal status) were recruited from the College of Dental Medicine, Rangsit University. There were 7 male and 10 female participants in the total age range of 45-68 years old. All participants had two or more sites of remaining periodontal probing depth (PPD) $\geq$ 5 mm and in bilateral quadrants with the presence of radiographic alveolar bone loss. All participants with uncontrolled systemic diseases or receiving medications, those who were allergic to tetracycline group and its derivatives, currently using antiseptic mouth rise within 1 day and drugs affecting periodontal status (anticonvulsant, immunosuppressant, calcium channel blocker, antibiotics), participants who had started orthodontic therapy, and smokers were excluded from the study.

Throughout the study, if any participant had any allergic symptoms such as gingival edema, angioedema, or dental abscess following the application of 2% Minocycline ointment, they would be withdrawn from the study. Any participant who had the desire to withdraw from the experiment due to any particular reason would also be excluded from the study. One participant was excluded from the study due to the smoking factor. Another participant was excluded due to his/her desire. Six participants were excluded due to failure to reach the first evaluation visit. The total 9 eligible participants; 3 males and 6 females, who met the inclusion criteria were determined at baseline and evaluation visit. There were resulting in 22 sites, which were selected and randomly allocated for 2% Minocycline HCL ointment application (test group) and non-application (control group).

The clinical parameters consist of periodontal probing depth (PPD), gingival margin (GM), and clinical attachment level (CAL) were recorded. PPD was measured by inserting the UNC-15 probe into the deepest part of the periodontal pocket where the resistance was felt on insertion from the pocket. Inserting in 6 sites including distobuccal, mid buccal, mesiobuccal, distolingual/distopalatal, midlingual/midpalatal, and mesiolingual/mesiopalatal. These measurements were rounded up to the nearest millimeter. CAL was calculated from PPD-GM.

The periodontal examination was performed by two well-trained Periodontists (S.B. and P.S.). These two examiners were blinded for all examinations. All parameters were recorded at baseline, then oral hygiene instruction was provided accordingly. Twenty-two sites were selected and randomly allocated for the test group (N=11) and the control group (N=11) by the following criteria. The teeth were paired in a group of two according to nearest CAL, PD, and tooth location respectively. The tooth that was left unpaired was not be included in the statistical analysis. 2% Minocycline ointment (Periocline®; GUIDOR, USA) was administered to the test sites. The tip of the applicator was inserted to the point of resistance in each pocket before the medication was administered. The amount of Periocline® administered should be sufficient to fill each pocket to the point of overflow. Tooth brushing, flossing, mouth rinsing, or eating were refrained for at least 2 hours immediately following administration of the medication. The ointment was applied in 11 sites of periodontal pocket at days 0, 14, and 28. The clinical data were obtained 4 weeks after the last administration of Periocline®.

For statistical analysis, data were entered into an Excel (Microsoft office 2020) database and were proofed for entry errors. The database was subsequently locked, imported into SPSS for Windows (SPSS Inc., version 25.0) formatted, and analyzed. Numerical data were summarized as means and SD, categorical data were summarized as frequency distribution. Shapiro-Wilk was used to test the distribution of data for PPD and CAL for both control and test group, to know which pair could be used in parametric or non-parametric statistical tests.

To compare the data between the two groups, the Mann-Whitney U test was used for baseline PPD, baseline CAL and evaluated PPD. To compare the data in each group, Wilcoxon Signed Rank Test was used for PPD and CAL. Paired t-test was used to compare CAL in the control group. The results were regarded as statistically significant when $p < 0.05$.

4. Results and Discussion

The measurement of PPD at the baseline showed no statistically significant difference between the test and the control group. At the evaluation, the control and test groups had PPD reductions equal to 0.82 mm and 1.09 mm, respectively. Both groups showed a statistically significant difference in the PPD reduction when compared with the baseline PPD (p = 0.014 for the control group and p = 0.015 for the test group). However, PPD at the evaluation between the two groups did not show a statistically significant difference.

The measurement of CAL at the baseline showed no statistically significant difference between the test and control groups. At the evaluation, CAL gain in the test group was 1.27 mm, showing a statistically significant difference from the baseline (p = 0.06). Interestingly, CAL gain in the control group was 0.64 mm, showing no statistically significant difference from the baseline CAL (Table 1).

Table 1 shows PPD and CAL at Baseline and Evaluation between the test and the control group.

	PPD (mm.)		PPD reduction (mm.)	*P*-value	CAL (mm.)		CAL gain (mm.)	*P*-value
	Baseline	**Evaluation**			**Baseline**	**Evaluation**		
Control group	6.09*±0.54	5.27*±1.01	0.82±0.75	0.014	6.09±1.51	5.45±1.75	0.64±1.03	0.067
Test group	5.55†±0.82	4.45†±0.82	1.09±1.04	0.015	5.82‡±1.40	4.55‡±1.29	1.27±0.79	0.006

* displays statistically significant PPD reduction in the control group (p<0.05) using Wilcoxon Signed Rank Test
† displays statistically significant PPD reduction in the test group (p<0.05) using Wilcoxon Signed Rank Test
‡ displays statistically significant CAL gain in the test group (p<0.05) using Wilcoxon Signed Rank Test

This study was conducted in periodontitis patients who had completed the hygenic phase of periodontal treatment. The results showed no statistically significant difference between the control and test groups of PPD, while there is a statistically significant difference improvement showed in the PPD reduction in both control and test groups from the baseline and 4 weeks after administration. The results were similar to an earlier study (Lu & Chei, 2005). The improvement of the PPD reduction might be due to the normal soft tissue healing rate (1-3 months) (Engler, Ramfjord, & Hiniker, 1966). However, the mean PPD reduction of the test group was greater than the control group, implying that the minocycline ointment may play a role in promoting soft tissue healing.

CAL showed no statistically significant difference between the control and test groups at the evaluation, which could be explained because the evaluation was recorded one month after the last administration while the hard tissue healing rate is around 4-6 months (Newman, 2015). The CAL results showed a statistically significant difference in the test group only when comparing with the baseline and at the evaluation, which may be due to Minocycline ointment that was utilized for a subgingival application consisting of a bioresorbable microsphere combined through delivery loaded system and is effective for a minimum of three days following the administration (Satomi et al., 1987). Minocycline also has a direct effect on anaerobes and spirochetes that are mostly found in a deep pocket. It causes a significant stimulation of osteoblastic cells, whereas long-term exposure of these cells to tetracyclines results in a proportional increase in the mineralized bone matrix (Garrido-Mesa, Zarzuelo, & Gálvez, 2013).

There was no incidence of drug allergy or complication reported in this study. However, there were limitations in this study such as a limited number of participants and a short period of evaluation time due to the Covid-19 outbreak.

5. Conclusion

The data suggested that subgingival administration of Minocycline HCL ointment after non-surgical periodontal treatment might be helpful in the PPD reduction and CAL gain within the first month after the administration. It showed more promising clinical benefits than conventional treatment alone. Further studies should be conducted on the long-term efficacy of Minocycline ointment. It could be an alternative treatment option to surgical intervention for periodontitis patients.

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7. References

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